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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,682	10/16/2001	Barney Scott Graham	VBLT:003US/SLH	6636

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/02/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,682	GRAHAM ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on July 14, 2003 in Paper No. 13 wherein claims 10, 12, and 21-50 are cancelled. Currently, claims 1-9, 11 and 13-20 are pending in this application.

Applicant's remarks filed on July 14, 2003 in Paper No. 13 with respect to the rejections of claims 9, 11, and 19-20 made under 35 U.S.C. 112 second paragraph for indefinite expression of record stated in the Office Action dated April 9, 2003 have been fully considered and found persuasive to remove the rejection as to claims 9, 11, and 19-20.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, for indefinite expressions "a subject" in claim 1, "severe combined immunodeficiency" in claim 4, "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" in claim 14, "a nucleoside analog composition" in claim 15, and "a protease inhibitor" in claim 16, for reasons of record stated in the Office Action dated April 9, 2003.

Applicant's remarks filed on July 14, 2003 in Paper No. 13 with respect to this rejection of claims 1-8, 11 and 13-20 made under 35 U.S.C. 112, second paragraph in

the previous Office Action have been fully considered but are not deemed persuasive for the following reasons.

Applicant's argument that "one skilled in the art would understand the bounds of the claims" and Applicant's assertion that one skilled in the art would understand these expressions "a subject" in claim 1, "severe combined immunodeficiency" in claim 4, "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" in claim 14, "a nucleoside analog composition", have been fully considered but not found persuasive. As noted in MPEP 2111, during patent examination, claims are given their **broadest** reasonable interpretation. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim, However, it is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) for example.

In the instant case, as discussed in the previous Office Action, the expression "a subject" in claim 1 renders the claims indefinite since the expression "a subject" is not seen to be clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret as to what is a subject herein, e.g., a cell, a mammal or an animal in the claim.

The expression "severe combined immunodeficiency" in claim 4 renders claim 4 indefinite since the term "severe" is a relative term. The expression "severe combined immunodeficiency" is not seen to be clearly defined in the specification. Even thought the phrase has been employed in US patent 6,091,000, one of ordinary skill in the art

could not interpret the metes and bounds as the patent protection desired in the *instant* invention.

As discussed above, one of ordinary skill in the art could not interpret the metes and bounds as the patent protection desired in the instant invention as to the expression "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" in claim 14, "a nucleoside analog composition" in claim 15, and "a protease inhibitor" in claim 16. Again, Applicant argues that other US patents employ these expressions. Nonetheless, this is not found persuasive since each application for patent is examined on its own merits, and patents are property and not available as precedent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Maziere et al. for reasons of record stated in the Office Action dated April 9, 2003.

Applicant's remarks filed on July 14, 2003 in Paper No. 13 with respect to this rejection of claims 1 and 8 made under 35 U.S.C. 102(b) in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art for the following reasons.

Applicant argues that Maziere does not disclose that a HMG-Coa reductase inhibitor prevents HIV infection of cells in a subject, specially *in vivo*. However, claims 1 and 8 are not limited to cells in a subject or in *vivo*. As discussed above, given the broadest reasonable interpretation of "a subject", the recitation "a subject" reads on a cell, cells, or in vitro. Therefore, said rejection is adhered to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 11, 13, 15-16, and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1449 submitted June 11, 2002) and Park et al. (C29, PTO-1449 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1449 submitted June 11, 2002) for reasons of record stated in the Office Action dated April 9, 2003.

Applicant's remarks filed on July 14, 2003 in Paper No. 13 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Applicant argues that the cited prior art fail to establish a necessary element required for a prima facie case of obviousness since the cited prior art "does not expressly disclose the employment of HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus such as respiratory syncytial virus (RSV) in a human, a non-human mammal, or a livestock animal" (as stated in the previous Office Action). However, claims 1-8 and 13-18 are not limited to cells in a subject or in *vivo*. As discussed above, given the broadest reasonable interpretation of "a subject", the recitation "a subject" reads on cell, cells, or in vitro.

Moreover, regarding *in vitro-in vivo* relationship, one of ordinary skill in the art would allow *in vitro* data to be used as a surrogate for *in vivo* behavior. Thus, one of ordinary skill in the art would employ HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus such as respiratory syncytial virus (RSV) in a human, a non-human mammal, or a livestock animal based on the *in vitro* testing results taught by the cited prior art.

Applicant also argues that the examiner has attempted to make a circuitous connection between the cited prior art but fails since each reference deals with distinct issues that only peripherally bear up on the claimed invention (emphasis added). Applicant also asserts that no person skilled in the art would have a reasonable expectation of success by combining the teachings of the cited prior art. Nevertheless, it must be recognized that any judgment on obviousness takes into account the knowledge which was within the level of ordinary skill at the time the claimed invention was made. As discussed in the previous Office Action, HMG-CoA reductase inhibitors

are known to be useful in a method for inhibiting infection of a cell by a virus such as HIV according to Maziere et al. Moreover, Park et al. teaches that HMG-CoA reductase inhibitors such as simvastatin and astrovastatin are useful in inhibiting of geranylgeranylation of RhoA GTPase. It is also known that the inhibition of RhoA GTPase would result in inhibiting RSV according to Pastey et al. Therefore, one of ordinary skill in the art would have reasonably expected that HMG-CoA reductase inhibitors would have a beneficial therapeutic effect in inhibiting infection of a cell by a virus such as RSV in a subject such as in a human, a non-human mammal, or a livestock animal, with a reasonable expectation of success, absent evidence to the contrary.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is obvious in view of the prior art.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1449 submitted June 11, 2002) and Park et al. (C29, PTO-1449 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1449 submitted June 11, 2002) for reasons of record stated in the Office Action dated April 9, 2003.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1449 submitted June 11, 2002) and Park et al. (C29, PTO-1449 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002) and Fisher et al. (C11, PTO-1449 submitted June 11, 2002) for reasons of record stated in the Office Action dated April 9, 2003.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1449 submitted June 11, 2002) and Park et al. (C29, PTO-1449 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002) and Gruber et al. (C17, PTO-1449 submitted June 11, 2002) for reasons of record stated in the Office Action dated April 9, 2003.

Applicant's remarks filed on July 14, 2003 in Paper No. 13 with respect to these three rejections made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as follows.

Again, claims 14, 17, and 18 are not limited to cells in a subject or in *vivo*. Regarding *in vitro-in vivo* relationship, one of ordinary skill in the art would allow *in vitro* data to be used as a surrogate for *in vivo* behavior, as discussed above.

In regard to the instant combinations, i.e., a HMG-CoA reductase inhibitor in combination with an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor; a HMG-CoA reductase inhibitor in combination with an antibody composition; a HMG-CoA reductase inhibitor in combination with ribavarin, in the claimed method, it has been held that it is prima facie obvious to combine two

compositions each of which is taught by the prior art to be useful for same purpose in order to form a third composition that is to be used for the very same purpose; idea of combining them flows logically from their having been individually taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. In the instant case, as discussed in the previous Office Action, one of ordinary skill in the art would have reasonably expected that combining a HMG-CoA reductase inhibitor and isoprenylation, an antibody composition, or ribavarin, known useful for the same purpose, i.e., inhibiting a viral infection such as RSV, in a composition to be administered would improve the therapeutic effect for treating a viral infection such as RSV, absent evidence to the contrary. Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

Further, Applicant's testing results shown in the Figures 1-11 and Example 2 of the specification herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. Figures 1-11 and Example 2 herein demonstrate only one particular HMG-CoA reductase inhibitor, lovastatin, diminishes a single virus, RSV replication in mice. Thus, the evidence in the working examples is not commensurate in scope with the claimed invention, i.e., any infection by any virus in claim 1 or those viruses recited in claim 8, and does not demonstrate criticality of a claimed range of HMG-CoA reductase inhibitors in the claimed method. See MPEP § 716.02(d). Furthermore, the record contains no evidence of nonobviousness or unexpected results for the combinations

recited in claims 14, 17, and 18 over the prior art. Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
September 24, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER
9/29/03